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Editorial

Resveratrol-based Nutraceuticals for the Management of Diabetes and Obesity: Real Therapeutic Potential or a mere Palliative?

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Editorial

It is well known that obesity and diabetes (more specifically, the type 2 diabetes mellitus, T2DM) are currently a growing public health problem, which involves several millions subjects in the World. Years ago, indeed, the term "*diabesity*" was coined highlighting not only the strong pathogenic relationship between obesity and T2DM, but also the pandemic aspect that link these two diseases. The increasing global prevalence of *diabesity* represents a grave concern in terms of public health and, at the same time, medical costs, resulting in a serious social economic issue.

Periodically, several scientific societies elaborate guidelines for the management of obesity and T2DM, mainly based on a particular interest in life-style and nutrition, as a useful strategy for prevention and treatment. In addition to the life-style intervention, a large number of drugs are currently available, and some of them (e.g. metformin or incretine-mimetic) are used both in case of diabetes and/or obesity. These pharmacological treatments, however, are not without side-effects. For this reason, the interest in natural drugs is nowadays emerging.

Beside the well-known phytotherapy, based on the use of medical herbs with documented beneficial effects on human health, a consolidated and growing interest is currently in nutraceutical. This term is a *crasis* between the words "nutrition" and "pharmaceutical", coined in the 1989 by Dr. S. DeFelice. Nutraceutical, thus, is the science studying chemical, composition and medical effects of the food- or animal-derived bioactive compounds, underling the strong influence of the diet on health. Nutraceutical, indeed, is currently recognized to be one the most important natural approach for management (mainly as add-on therapy to the common treatments) and the prevention of several pathologies, acting "beyond diet, before drugs" as stated in 2012 by Prof. E. Novellino [1].

Nowadays a large number of evidence-based data regarding the effects of single or group of food-derived bioactive compounds are available in scientific literature, pointing out the interest of scientific research in nutraceuticals. In particular, several in vitro, animal-based and in vivo studies were carried out demonstrating the effects of nutraceutical in managing obesity and/or diabetes. As an example, we demonstrated that polyphenols from white tea exhibited a strong activity in reducing glucose uptake in HepG2 cell lines [2]. Moreover, it was proposed a possible anti-diabetic or anti-obesity effect of the bitter compounds contained in beer, which may act stimulating the intestinal bitter taste receptors, resulting in increasing the incretine release [3], but further investigation are needed.

Beside this evidence, in this document we would like to focus your attention to the role of resveratrol (RSV) on *diabesity*. RSV is the most representative polyphenol contained in skin of grapes and wine. Several beneficial effects are attributed to RSV and, among these, the well- and historically-known cardio protection. Interestingly, RSV has been reported to exert anti-diabetes and anti-obesity effects [4]. Although it has not been too much stressed, studies demonstrated an important mechanism of action by which RSV can act in prevention and management of *diabesity*: the activation of the 5' AMP-activated protein kinase (AMPK) [5-8], a Ser-Thr kinase strongly involved in regulation of cellular and glucose metabolism [9], target of anti-diabetic drugs, such as metformin [10,11]. This AMPK activation is the main target for the RSV metabolic effect [12], resulting in

a) Stimulating the glucose uptake in L6 myotubes [13,14]

b) Inhibiting adipocyte differentiation [14]

c) Improving glucose homeostasis and symptoms in animal

model of gestational diabetes [15]

d) Promoting formation of brown adipocytes and exerting thermogenic effects [16]

With this editorial, we would like to propose a start point for discussion and an input for further investigations about the role of RSV-based nutraceuticals, which have been shown to be not a mere palliative but a novel and promising natural approach for the management of *diabesity*. We hope this Journal will encourage the scientific discussion regarding the role of nutraceutical sciences in metabolic diseases focusing on the evidences, safety and absence of side-effects, enlarging the knowledge of physician on this issue.

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